PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP2004/006069	04.06.2004	06.06.2003

International Patent Classification (IPC) or both national classification and IPC
C12N15/82, A01H5/00

Applicant
ICON GENETICS AG

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:

European Patent Office - P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk - Pays Bas
Tel. +31 70 340 - 2040 Tx: 31 651 epo nl
Fax: +31 70 340 - 3016

Authorized Officer

Holtorf, S

Telephone No. +31 70 340-2627

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/EP2004/006069

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was field, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. II Priority

1. ☒ The following document has not been furnished:

   ☒ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).

   ☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

   Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	9,14-17,19-23,25,26,29
	No:	Claims	1-8,10-13,18,24,27,28,30-37
Inventive step (IS)	Yes:	Claims	9,14-17,19-23,25,26,29
	No:	Claims	1-8,10-13,18,24,27,28,30-37
Industrial applicability (IA)	Yes:	Claims	1-37
	No:	Claims	

2. Citations and explanations

see separate sheet

1. The following document is considered relevant for the current application:

D1: EP1048734
D2: Bayley, C., et al.; 1992, Plant Molecular Biology; Vol.18, pp. 353-361
D3 WO9604393
D4: WO983711

Re Item V.

2. Novelty and **Clarity** (Art. 33(2) and Art. 6 PCT)

2.1 The current application is dealing with the provision of a method for the safe and high yield expression of a product of interest in hybrid seeds. The expression of the gene of interest is thereby controlled by integrating a viral provector harbouring said gene of interest into the genome of a first plant and crossing said first plant to a second parental plant that harbours a component (here: the phiC31 Integrase) capable of generating an active replicon (here: BGMV, wheat dwarf virus and TMV) that leads to the expression of the gene of interest in the F1-seeds. Either through the expression of the viral replicon leading to impairment of a normal seeding development or by the provision of an additional lethal split-gene construct (here: Barnase) provided in either of the parental plants, the spread of the F1-seed and genetic contamination is prevented.

2.2 As currently drafted, Claim 1 refers to a general method of producing a product by "hybridising" a first and second "transgenic parental plant" to generate a "genetic endowment" by combining the first and second "partial genetic endowments".
The "transgenic plants" and the "genetic endowments" are not further defined and as currently drafted, any method for the production of any product in any F1-plant generated by ordinary classical breeding techniques (or even somatic "hybridisation" of protoplasts) and not involving any genetic engineering step would fulfill the wording of this claim. Such methods and also such plants and F1-seeds are already known in the prior art and consequently, claim 1 lacks novelty over the prior art with respect to Art. 33(2) PCT.
The same objection applies to claims 2-8,30-37. In its broadest possible sense, even claims 9-23 can be interpreted of referring to virus-infected, ordinary plants that are crossed.

2.3 Furthermore, if viral infection is severe, said seeds would eventually not survive due to "the tissue-specific expression of a toxic substance or protein interfering with normal plant development" (see claim 28) and would result in the F1 seeds incapable of sexual reproduction (see claims 24-28).

3. Inventive Step (Art.33 (3) PCT)

3.1 With the claims as they stand it is very hard to identify the closest prior art and even identify the problem underlying the invention.

3.2 Methods for using two parental plants harbouring two different chimeric constructs which upon crossing of said plants form an active gene of interest or an active product of interest are already known, see D1. Dual recombinase vector systems are already known in the prior art, see D2 and D3. Furthermore, the split-gene technology is also known, see D4.
It appears that the specific combination of an inactive viral provector harbouring the gene of interest provided in a 1st plant followed by the activation of said gene of interest upon crossing to a 2nd plant harbouring a recombinase under control of a seed-specific promoter and which leads to high yield expression of the product of interest and also to a an F1-seed that is incapable of sexual reproduction due to either viral replication or the coexpression of a lethal gene, is not obvious and inventive according to Art.33 (3) PCT.